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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : A61K 7/42, C07D 249/20	A1	(11) International Publication Number: <b>WO 98/23252</b> (43) International Publication Date: 4 June 1998 (04.06.98)
(21) International Application Number: PCT/EP97/06330 (22) International Filing Date: 13 November 1997 (13.11.97) (30) Priority Data: 2885/96 22 November 1996 (22.11.96) CH (71) Applicant (for all designated States except US): CIBA SPECIALTY CHEMICALS HOLDING INC. [CH/CH]; Klybeckstrasse 141, CH-4057 Basel (CH). (72) Inventors; and (75) Inventors/Applicants (for US only): LUTHER, Helmut [DE/DE]; Tüllingerweg 3a, D-79639 Grenzach-Wyhlen (DE). REINEHR, Dieter [DE/DE]; Wolfsheule 10, D-79400 Kandern (DE). ZINK, Rudolf [CH/CH]; Nelkenstrasse 19, CH-4106 Therwil (CH). (74) Common Representative: CIBA SPECIALTY CHEMICALS HOLDING INC.; Patentabteilung, Klybeckstrasse 141, CH-4057 Basel (CH).	(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).  Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	
(54) Title: USE OF SELECTED BENZOTRIAZOLE DERIVATIVES FOR PROTECTING HUMAN AND ANIMAL SKIN AND HAIR FROM THE HARMFUL EFFECTS OF UV RADIATION		
(57) Abstract <p>A description is given of the use of benzotriazole derivatives of formula (1) wherein R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub>, X, L and p are as claimed in claim 1. These compounds are distinguished by having good substantivity for human hair while at the same time effectively protecting hair and skin against UV radiation.</p> <div style="text-align: center;"> <p style="text-align: right;">(1)</p> </div>		

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Use of selected benzotriazole derivatives for protecting human and animal skin and hair from the harmful effects of UV radiation

The present invention relates to the use of selected benzotriazole derivatives for protecting human and animal hair and skin from the harmful effects of UV radiation.

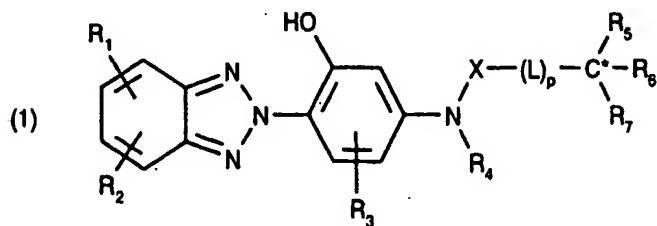
It is known that UV radiation having a wavelength of 285 to 400 nm causes or accelerates a very wide range of skin damages in humans, for example erythemas, accelerated skin ageing, phototoxic and photoallergic reactions and the like. If human hair is exposed to sunlight over a prolonged period of time it may be damaged in different ways. Under the influence of sunlight, dyed hair can change its colour and shade. Blond hair turns yellowish. The hair surface becomes rougher and at the same time drier. Furthermore, the hair gradually loses its sheen.

Chemical compounds in the form of cosmetic formulations recommending themselves for the topical protection of human skin and of the hair surface are therefore those which are able to reduce or prevent the mentioned harmful effects of UV radiation.

Surprisingly, it has now been found that specific benzotriazole derivatives have excellent substantivity for human hair while at the same time providing effective UV protection for hair and human skin.

Accordingly, this invention relates to the use of selected benzotriazole derivatives for protecting human and animal hair and skin from the harmful effects of UV radiation.

The selected benzotriazole compounds are compounds of formula



wherein

R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> are each independently of one another hydrogen; straight-chain or branched C<sub>1</sub>-C<sub>22</sub>alkyl; hydroxy; carboxy; carbo-C<sub>1</sub>-C<sub>22</sub>alkoxy; nitro; C<sub>2</sub>-C<sub>22</sub>alkylcarbonylamino; C<sub>5</sub>-C<sub>8</sub>cycloalkyl; carbamoyl; sulfonyl; sulfamoyl; sulfonamido; C<sub>2</sub>-C<sub>22</sub>alkylcarbonyloxy; cyano; halogen; C<sub>6</sub>-C<sub>12</sub>aryl or C<sub>4</sub>-C<sub>12</sub>heteroaryl which is unsubstituted or substituted by one or several C<sub>1</sub>-C<sub>4</sub>alkyl; C<sub>7</sub>-C<sub>10</sub>aralkyl which is unsubstituted or substituted by one or several C<sub>1</sub>-C<sub>4</sub>alkyl; C<sub>8</sub>-C<sub>12</sub>aryloxy; or a radical of formula



wherein

A<sub>1</sub> is straight-chain or branched C<sub>1</sub>-C<sub>8</sub>alkyl; C<sub>5</sub>-C<sub>8</sub>cycloalkyl; C<sub>6</sub>-C<sub>12</sub>aryl which is unsubstituted or substituted by one or several C<sub>1</sub>-C<sub>4</sub>alkyl; or C<sub>7</sub>-C<sub>10</sub>aralkyl which is unsubstituted or substituted by one or several C<sub>1</sub>-C<sub>4</sub>alkyl;

m<sub>1</sub> is 1 to 10;

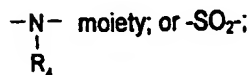
Q is -O-; -S-; or -NH-; or

R<sub>1</sub> and R<sub>2</sub>, together with the benzene ring of the benzotriazole, are a C<sub>5</sub>-C<sub>18</sub>aryl ring or a C<sub>4</sub>-C<sub>18</sub>heteroaryl ring, which rings are unsubstituted or substituted by C<sub>1</sub>-C<sub>22</sub>alkyl or C<sub>1</sub>-C<sub>22</sub>alkoxy;

R<sub>4</sub> is hydrogen; C<sub>1</sub>-C<sub>22</sub>alkyl which is unsubstituted or substituted by 1 to 5 halogen atoms and/or which is interrupted by a -C(O)-O- or -SO<sub>2</sub>-O- group;

R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> are each independently of one another hydrogen; halogen; cyano; straight-chain or branched C<sub>1</sub>-C<sub>22</sub>alkyl; straight-chain or branched C<sub>1</sub>-C<sub>22</sub>alkoxy; C<sub>6</sub>-C<sub>12</sub>aryl; straight-chain or branched C<sub>1</sub>-C<sub>22</sub>thioalkyl; mono- or di-C<sub>1</sub>-C<sub>22</sub>alkylamino; mono- or di-C<sub>6</sub>-C<sub>12</sub>aryl amino; R<sub>5</sub> ≠ R<sub>6</sub> ≠ R<sub>7</sub>;

X is  $\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{O}- \end{array}$ , the carbonyl carbon atom being bound to the nitrogen atom of the



L is a divalent radical consisting of 1 to 20 atoms; and

p is 0 or 1.

Straight-chain and branched C<sub>1</sub>-C<sub>22</sub>alkyl is typically methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, isobutyl, t-butyl, 2-ethylbutyl, n-pentyl, isopentyl, 1-methylpentyl, 1,3-dimethylbutyl, n-hexyl, 1-methylhexyl, n-heptyl, isoheptyl, 1,1,3,3-tetramethylbutyl, 1-methylheptyl, 3-methylheptyl, n-octyl, 2-ethylhexyl, 1,1,3-trimethylhexyl, 1,1,3,3-tetramethylpentyl, nonyl, decyl,

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heptyl, 3-methylheptyl, n-octyl, 2-ethylhexyl, 1,1,3-trimethylhexyl, 1,1,3,3-tetramethylpentyl, nonyl, decyl, undecyl, 1-methylundecyl, dodecyl, 1,1,3,3,5,5-hexamethylhexyl, tridecyl, tetradecyl, pentadecyl, hexadecyl, heptadecyl, octadecyl or eicosyl.

C<sub>5</sub>-C<sub>8</sub>Cycloalkyl is typically cyclopentyl, cycloheptyl, cyclooctyl and, in particular, cyclohexyl.

Examples of C<sub>6</sub>-C<sub>12</sub>aryl to be mentioned are, in particular, phenyl, naphthyl and biphenyl.

Typical examples of C<sub>7</sub>-C<sub>10</sub>aralkyl are benzyl, phenethyl, α-methylphenethyl or α,α-dimethylbenzyl.

"Alkylene" in formula (1a) is a divalent alkylene group containing 2 to 5, preferably 2 to 4 carbon atoms. It is preferably the -CH<sub>2</sub>-CH<sub>2</sub>-; -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-;

-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-;  $\begin{array}{c} \text{CH}_3 \\ | \\ -\text{CH}-\text{CH}_2-\text{CH}_2- \end{array}$ ; or  $\begin{array}{c} -\text{CH}_2-\text{CH}-\text{H}_2\text{C}- \\ | \\ \text{H}_3\text{C} \end{array}$  group. Of these alkylene

groups, the -CH<sub>2</sub>-CH<sub>2</sub>- and the

$\begin{array}{c} \text{CH}_3 \\ | \\ -\text{CH}_2-\text{CH}- \end{array}$  group are very particularly preferred.

Halogen is fluoro, bromo or, preferably, chloro.

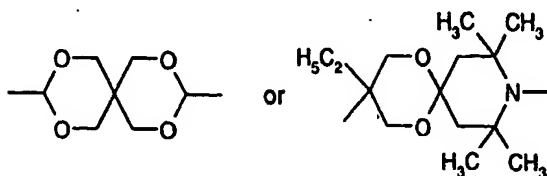
The compound of formula (1) is preferably a 60:40 to 40:60 mixture of two enantiomers relative to the asymmetrical C\* atom.

L can consist, in particular, of 1 to 20 atoms and can be a straight-chain or branched alkylene group which may be interrupted by 1 to 5 oxygen, sulfur or nitrogen atoms or by a -C(O)-O- group which is unsubstituted or substituted by C<sub>1</sub>-C<sub>10</sub>alkoxy, C<sub>1</sub>-C<sub>10</sub>alkylcarbonyloxy, C<sub>1</sub>-C<sub>10</sub>alkyl sulfide, amino, mono-C<sub>1</sub>-C<sub>10</sub>alkylamino, di-C<sub>1</sub>-C<sub>10</sub>alkylimino or halogen; or the divalent radical of a 4- to 6-membered alicyclic ring or of a heterocyclic ring containing 1 to 3 hetero atoms.

Illustrative examples of alicyclic and heterocyclic radicals are heterocyclic radicals containing cyclohexylene, pyrrolidinylene, tetrahydrofuranylene, tetrahydrothienylene,

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piperidinylene, pyrrolylene, furylene, thienylene, pyridylene or spiro ethers, for example



In particular, L may also be a methine group which is unsubstituted or substituted by C<sub>1</sub>-C<sub>12</sub> alkyl or C<sub>1</sub>-C<sub>12</sub>alkoxy, amino, mono- or di-C<sub>1</sub>-C<sub>6</sub>alkylamino or halogen, wherein C<sub>1</sub>-C<sub>12</sub>alkyl or C<sub>1</sub>-C<sub>12</sub>alkoxy may be interrupted by 1 or 2 oxygen atoms.

Typical examples of L defined as divalent radicals are:

- alkylene groups, such as -CH<sub>2</sub>-; CH<sub>2</sub>-CH<sub>2</sub>-; -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-;


-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-;  $\begin{array}{c} \text{CH}_3 \\ | \\ -\text{CH}-\text{CH}_2-\text{CH}_2- \end{array}$ ; or the  $\begin{array}{c} -\text{CH}_2-\text{CH}-\text{H}_2\text{C}- \\ | \\ \text{H}_3\text{C} \end{array}$  group. Of these

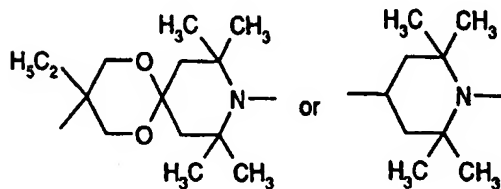
alkylene groups, the -CH<sub>2</sub>- and the -CH<sub>2</sub>-CH<sub>2</sub>- group are very particularly preferred.

- Radicals containing oxygen atoms or -C(O)-O- groups, such as

-CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-O-; -(CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-O)<sub>2</sub>-; -CH<sub>2</sub>-C(O)OCH<sub>2</sub>-;

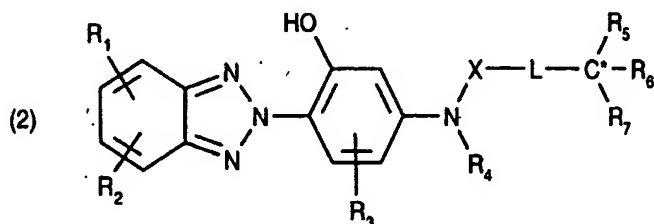
-CH<sub>2</sub>-C(O)OCH<sub>2</sub>CH(OCOCH<sub>3</sub>)CH<sub>2</sub>O-;

- heterocyclic radicals, such as ,



R<sub>5</sub>, R<sub>6</sub>, R<sub>7</sub> in formula (1) are preferably each hydrogen; or, independently of one another, straight-chain or branched C<sub>1</sub>-C<sub>22</sub>alkyl.

According to this invention, it is very particularly preferred to use benzotriazole derivatives of formula



wherein

$R_1$  and  $R_2$  are each independently of one another hydrogen; halogen;  $C_1$ - $C_5$ alkyl;  $C_1$ - $C_5$ alkoxy; mono- or di- $C_1$ - $C_5$ alkylamino; or  $C_1$ - $C_5$ alkyl sulfide;

$R_3$  is hydrogen; hydroxy; or halogen;

$R_4$  is hydrogen;  $C_1$ - $C_5$ alkyl which is unsubstituted or substituted by 1 to 5 halogen atoms and/or which may be interrupted by a  $-C(O)-O-$  or  $-SO_2-O-$  group;

$L$  is a straight-chain or branched alkylene group which may be interrupted by 1 to 5 oxygen atoms or by a  $-C(O)-O-$  group which may be substituted by  $C_1$ - $C_{10}$ alkoxy or  $C_1$ - $C_{10}$ alkylcarbonyloxy; and

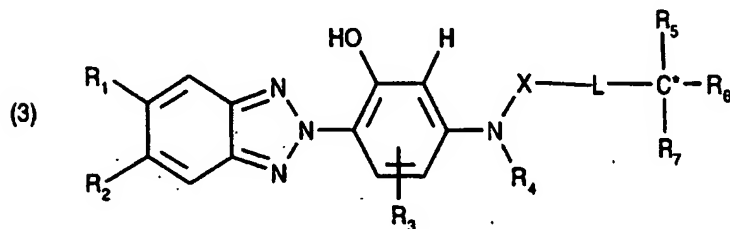
$R_5$ ,  $R_6$ ,  $R_7$  are each independently of one another hydrogen or  $C_1$ - $C_{10}$ alkyl;  $R_5 \neq R_6 \neq R_7$ ;

and

$X$  is  $-\overset{\overset{O}{\parallel}}{C}-O-$ , the carbonyl carbon atom being bound to the nitrogen atom of the  $-\overset{\overset{R_4}{|}}{N}-$

moiety; or  $-SO_2-$ .

Very particularly preferred benzotriazole derivatives are those of formula



wherein

$R_3$  is hydrogen; halogen or hydroxy;

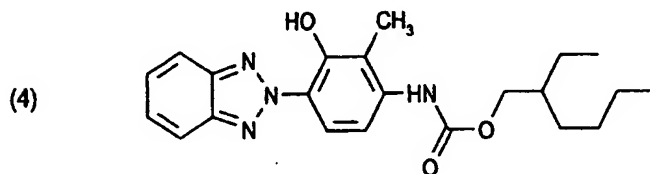
$R_4$  is hydrogen;  $C_1$ - $C_5$ alkyl which is unsubstituted or substituted by 1 to 5 halogen atoms and/or which may be interrupted by a  $-C(O)-O-$  or  $-SO_2-O-$  group;

$R_5, R_6, R_7$  are each independently of one another hydrogen or  $C_1$ - $C_{10}$ alkyl;  $R_5 \neq R_6 \neq R_7$ ;

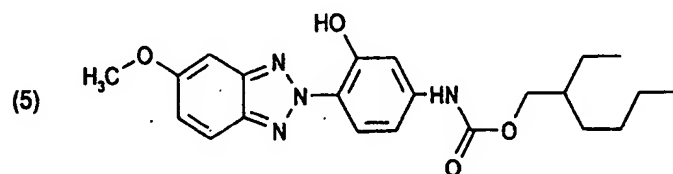
$L$  is a straight-chain or branched alkylene group which may be interrupted by 1 to 5 oxygen atoms or by a  $-C(O)-O-$  group which may be substituted by  $C_1$ - $C_{10}$ alkoxy or  $C_1$ - $C_{10}$ alkylcarbonyloxy; and

$X$  is  $\begin{array}{c} O \\ || \\ -C-O- \end{array}$ , the carbonyl carbon atom being bound to the nitrogen atom of the  $\begin{array}{c} -N- \\ | \\ R_4 \end{array}$  moiety; or  $-SO_2-$ .

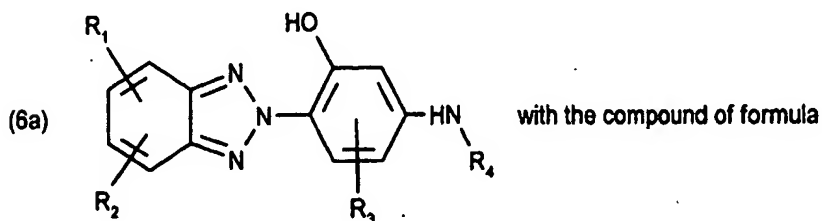
Some of the benzotriazole derivatives of formula (1) are known compounds. Some of them are, however, novel compounds. These novel compounds correspond to formula



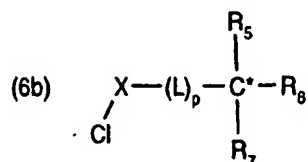
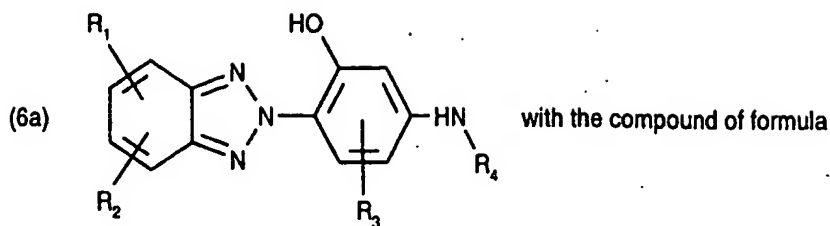
or to formula



The benzotriazole derivatives of formula (1) can be prepared by reacting the chromophore of formula







$R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$ ,  $R_5$ ,  $R_6$ ,  $R_7$ ,  $X$ ,  $L$  and  $p$  in this case have the meanings given for the compounds of formula (1).

A detailed description of the preparation may be found in US-A-5,500,332.

The compound of formula (6a) may be prepared starting from *o*-nitroaniline, 4-chloro-2-nitroaniline and *m*-amino- or *m*-aminoalkyl-substituted phenols by generally known preparation methods which are described, inter alia, in US-A-3,813,255. 2-(2'-Hydroxy-4'-aminophenyl)benzotriazole, for example, can be prepared by reacting 2-nitrobenzenediazonium chloride with 3-aminophenol and by subsequent reductive ring closure of the azo dye to the desired benzotriazole.

The benzotriazole derivatives of formula (1) are known as UV absorbers for technical applications, e.g. for plastic materials, paints systems and films, natural or synthetic resins, waxy materials or rubber. They are also, surprisingly, suitable for protecting human and animal skin and hair from the harmful effects of UV radiation and can therefore be used as light stabilisers in cosmetic, pharmaceutical and veterinary preparations. As water-soluble compounds they are usually used in dissolved form.

Accordingly, this invention also relates to a cosmetic preparation comprising at least one compound of formula (1) as well as cosmetically compatible carriers or auxiliaries.

The novel cosmetic preparation preferably comprises 0.25 to 15 % by weight, based on the total weight of the composition, of a benzotriazole derivative of formula (1).

In addition to the novel UV absorbers, the cosmetic formulation for hair can also contain one or more than one further UV protective of the following substance classes:

1. p-aminobenzoic acid derivatives, typically 2-ethylhexyl 4-dimethylaminobenzoate;
2. salicylic acid derivatives, typically 2-ethylhexyl salicylate;
3. benzophenone derivatives, typically 2-hydroxy-4-methoxybenzophenone and its 5-sulfonic acid derivative;
4. dibenzoylmethane derivatives, typically 1-(4-tert-butylphenyl)-3-(4-methoxyphenyl)-propane-1,3-dione;
5. diphenylacrylates, typically 2-ethylhexyl-2-cyano-3,3-diphenylacrylate and 3-(benzofuranyl)-2-cyanoacrylate;
6. 3-imidazol-4-yl-acrylic acid and 3-imidazol-4-yl-acrylate;
7. benzofuran derivatives, preferably 2-(p-aminophenyl)benzofuran derivatives, disclosed in EP-A-582,189, US-A-5,338,539, US-A-5,518,713 and in EP-A-613,893;
8. polymeric UV absorbers, such as the benzylidenemalonate derivatives described, inter alia, in EPA-709,080;
9. cinnamic acid derivatives, typically the 2-ethylhexyl 4-methoxycinnamate or isoamylate or cinnamic acid derivatives disclosed, inter alia, in US-A-5,601,811 and WO 97/00851;
10. camphor derivatives, typically 3-(4'-methyl)benzylidenebornan-2-one, 3-benzylidenebornan-2-one, N-[2(and 4)-2-oxyborn-3-ylidenemethyl]benzyl]acrylamide polymer, 3-(4'-trimethylammonium)benzylidenebornan-2-one methyl sulfate, 3,3'-(1,4-phenylenedimethine)-bis(7,7-dimethyl-2-oxo-bicyclo-[2.2.1]heptane-1-methansulfonic acid) and the salts thereof, 3-(4'-sulfo)benzylidenebornan-2-one and the salts thereof;
11. trianilino-s-triazine derivatives, typically 2,4,6-trianiline-(p-carbo-2'-ethyl-1'-oxi)-1,3,5-triazines as well as the UV absorbers disclosed in US-A-5,332,568, EP-A-517,104, EP-A-507,691, WO 93/17002 and EP-A-570,838;
12. 2-hydroxyphenylbenzotriazole derivatives;
13. 2-phenylbenzimidazole-5-sulfonic acid and the salts thereof;
14. menthyl-o-aminobenzoate;
15. TiO<sub>2</sub> (coated differently), ZnO and mica.

The cosmetic formulations can be prepared by physically mixing the UV absorber(s) with the auxiliary by conventional methods, such as by simply stirring the individual components together.

The cosmetic formulations of this invention can be formulated as water-in-oil or oil-in-water emulsion, as oil-in-alcohol lotion, as vesicular dispersion of a ionic or nonionic amphiphilic lipid, as gel, solid stick or as aerosol formulation.

As water-in-oil or oil-in-water emulsion, the cosmetically compatible auxiliary preferably comprises 5 to 50% of an oil phase, 5 to 20% of an emulsifier and 30 to 90% of water. The oil phase can contain any oil suitable for cosmetic formulations, for example one or several hydrocarbon oils, wax, natural oil, silicone oil, fatty acid ester or fatty alcohol. Preferred mono- or polyols are ethanol, isopropanol, propylene glycol, hexylene glycol, glycerol and sorbitol.

To prepare the novel cosmetic formulations it is possible to use any conventionally usable emulsifier, typically one or several ethoxylated esters of natural derivatives, such as polyethoxylated ester of hydrogenated castor oil; or a silicone oil emulsifier, such as silicone polyol; a free or ethoxylated fatty acid soap; an ethoxylated fatty alcohol; a free or ethoxylated sorbitan ester; an ethoxylated fatty acid; or an ethoxylated glyceride.

The cosmetic formulations may also contain other components, such as emollients, emulsion stabilisers, skin moisturisers, suntan promoters, thickeners, such as xanthan, moisture retention agents, such as glycerol, preservatives, fragrances and colourants.

The novel cosmetic formulations are distinguished by excellently protecting human skin against the harmful effects of sunlight over a prolonged period of irradiation.

The UV absorbers of formula (1) used according to this invention are particularly suitable for protecting human hair from the harmful effects of UV radiation.

The UV absorbers are distinguished by

- having high substantivity for human hair, and
- guaranteeing high UV protection for hair.

It is possible to use, for example, the following cosmetic formulations for hair:

- a<sub>1</sub>) spontaneously emulsifying stock formulations, consisting of the UV absorber, PEG-6 C<sub>10</sub>oxoalcohol and sorbitan esquioleate, which is charged with water and any quaternary ammonium compound, such as 4% minkamidopropyldimethyl-2-hydroxyethyl ammonium chloride or Quaternium 80;
- a<sub>2</sub>) spontaneously emulsifying stock formulation, consisting of the UV absorber, tributyl citrate and PEG-20 sorbitan monooleate, which is charged with water and any quaternary ammonium compound, such as 4% minkamidopropyldimethyl-2-hydroxyethyl ammonium chloride or Quaternium 80;
- b) quat-doped solutions of the UV absorber in butyl triglycol and tributyl citrate;
- c) dispersions of micronised UV absorbers obtained by known methods (precipitation from solutions or mixtures of solutions, grinding), having an average diameter of 0.05 - 1.0 µm in APG (e.g. Plantaren), and a quat (e.g. minkamidopropyldimethyl-2-hydroxyethyl ammonium chloride) in an aqueous formulation;
- d) mixtures or solutions of the UV absorber with n-alkylpyrrolidone.

This invention also relates to a method of treating human hair to protect it from the harmful effects of UV radiation. This method comprises treating hair with a shampoo, lotion or gel, or with an emulsion for rinsing, before or after shampooing, before or after dyeing or removing dye, before or after a perming or straightening process; with a lotion, foam or gel for setting; with a lotion, foam or gel for brushing or waving; with a hair lacquer; with a composition for perming or straightening hair, for dyeing or removing dye, which shampoo, lotion, gel, emulsion, foam, hair lacquer or composition for perming, straightening, dyeing or removing dye comprises at least one benzotriazole compound of formula (1).

The following non-limitative Examples illustrate the invention in more detail.

#### Preparation of novel compounds

##### Example 1:

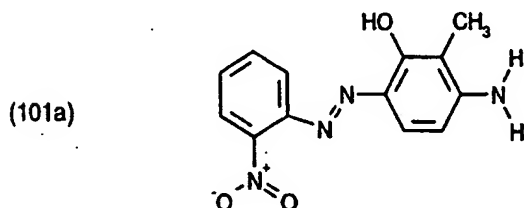
3.3g of o-nitroaniline are diazotised and the diazonium compound so obtained is coupled to a solution of 4.1g of 3-amino-o-cresol in 60ml of water and 3.3 g of concentrated hydrochloric acid. In the course of the coupling reaction, the coupling suspension is diluted with

The following non-limitative Examples illustrate the invention in more detail.

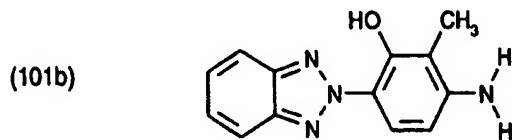
#### Preparation of novel compounds

##### Example 1:

3.3g of o-nitroaniline are diazotised and the diazonium compound so obtained is coupled to a solution of 4.1g of 3-amino-o-cresol in 60ml of water and 3.3 g of concentrated hydrochloric acid. In the course of the coupling reaction, the coupling suspension is diluted with 250ml of water to improve the stirrability and is then stirred for 3 hours at 25°C, and the red suspension is collected by suction filtration. To purify the water-moist product it is stirred in 250ml of ethanol at 25°C for 1 hour and then filtered. The red azo dye of formula

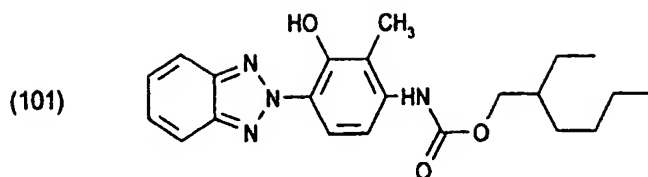


so obtained is made into a slurry in 100ml of water and 28.8ml of 10 N sodium hydroxide solution at 25°C. Subsequently, 6g of zinc dust are added and the mixture is stirred for 16 hours at 25°C. This mixture is then heated to 40°C and another 2g of zinc dust and 2ml of 10 N sodium hydroxide solution are added. After stirring for 4 hours at 35-40°C, the yellow-green suspension is clarified by filtration using a filter auxiliary and neutralised from pH 13.8 to pH 6.6 with 16ml of concentrated hydrochloric acid. A beige product precipitates which, after stirring for 1 hour at 25°C, is isolated by filtration. After recrystallising three times from isopropyl alcohol, 1200mg of a pure product of formula



are obtained having a melting point of 236-236.5°C.

1000mg of this compound are made into a slurry in 30ml of ethyl acetate and are then charged with 2ml of water and 0.53g of potassium hydrogencarbonate and cooled to 10°C.

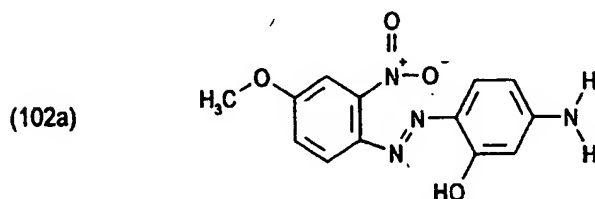


The melting point is 124-125°C.

$\epsilon = 24139 \text{ l} / (\text{mol} / \text{cm})$  (in ethanol);  $\lambda_{\text{max}} = 340 \text{ nm}$ .

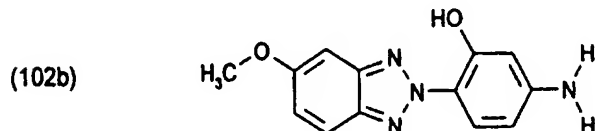
#### Example 2:

67g of 4-methoxy-2-nitroaniline are diazotised in water in conventional manner and the diazonium compound so obtained is then coupled to 64.4g of 3-aminophenol at pH 3. The red azo dye of formula



is isolated and processed in a water-moist state.

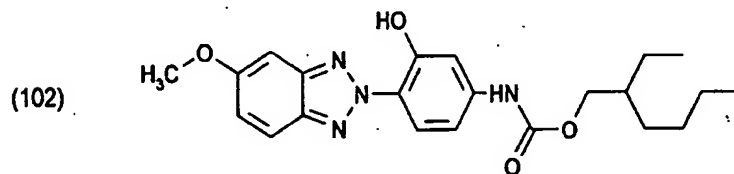
The above azo dye is made into a slurry in 1000ml of water and 140ml of 10N sodium hydroxide solution at 25°C, to which 90g of zinc dust are then added in portions (over 1 hour), the temperature rising to 36°C. After stirring for 15 hours, the temperature drops to 25°C. The mixture is heated to 40°C and another 55g of zinc dust and 100ml of 10 N sodium hydroxide are then added in portions. The reaction is followed by thin-layer chromatography and is complete after 3 hours and at 40°C. The reaction mixture is clarified by filtration and the filtrate is adjusted to pH 6.4 with 250ml of concentrated hydrochloric acid and the precipitated product is filtered after 1 hour at 25°C. After two recrystallisations, 5.7 g of the pure product of formula



are obtained.

Melting point: 190-191°C.

3.84g of this compound are stirred into 100ml of ethyl acetate and are then charged with 8ml of water and 1.92 g of potassium hydrogencarbonate and cooled to 10°C. 3g of 2-ethylhexyl chloroformate are then added dropwise over 45 minutes. The temperature is allowed to rise to 25°C. After stirring for 4 hours, the phases are separated in a separating funnel and the acetate phase is extracted with a mixture of 120ml of water, 16ml of 2N sulfuric acid and 60ml of 10% brine. After separation, the product is clarified by filtration with activated carbon, dried with sodium sulfate and concentrated at reduced pressure. The solidified residue is pounded together with 200ml of water and filtered. Recrystallisation from 100ml of ethanol affords 3.3g of the enantiomer mixture of formula



Melting point: 122-124°C.

$\epsilon = 32152 \text{ l}/(\text{mol}/\text{cm})$  in ethanol;  $\lambda_{\text{max}} = 353 \text{ nm}$ .

Application Examples

Example 3: Composition of a cosmetic formulation with the benzotriazole compound of formula (101) from Example 1 (the individual components are named according to CTFA or INCI):

(a <sub>1</sub> ) cetareth 6 (and) stearyl alcohol	2.0%
(a <sub>2</sub> ) cetareth 25	2.0%
(a <sub>3</sub> ) cetaryl alcohol	5.0%
(a <sub>4</sub> ) caprylic/capric triglyceride	5.0%
(a <sub>5</sub> ) cetaryl octanate	10.0%
(a <sub>6</sub> ) Vaseline	5.0%
(a <sub>7</sub> ) compound of formula (101)	4.0%
(b <sub>1</sub> ) propylene glycol	3.0%
(b <sub>2</sub> ) carbopol 934	0.2%
(b <sub>3</sub> ) H <sub>2</sub> O	63.53%
(c) triethanol amine	0.27%

Components (a<sub>1</sub>)-(a<sub>7</sub>) (= phase A) and (b<sub>1</sub>)-(b<sub>3</sub>) (= phase B) are heated to 75-80°C. Phase B is then added to phase A and homogenised. Component (c) (= phase C) is then added and again homogenised.

This O/W emulsion has a sunscreen factor of 4.

The UVA/UVB ratio is 1.23, which is a very good value for a cosmetic sunscreen formulation.

The sunscreen factors are determined according to the method of Diffey and Robson, J. Soc. Cosmet. Chem. 40, 127 - 133 (1989) using an SPF (sunproof factor) analyser (Optometrix, SPF 290).



**Example 4:** Composition of a cosmetic formulation with the benzotriazole compound of formula (102) from Example 2 (the individual components are named according to CTFA or INCI):

(a <sub>1</sub> ) dimethicone	2.0 %
(a <sub>2</sub> ) isopropyl myristate	9.0 %
(a <sub>3</sub> ) stearyl alcohol	10.0 %
(a <sub>4</sub> ) stearic acid	4.0 %
(a <sub>5</sub> ) octyl methoxycinnamate	4.0 %
(b <sub>1</sub> ) triethanolamine	1.2 %
(b <sub>2</sub> ) carbomer 934 (1%)	5.0 %
(b <sub>3</sub> ) H <sub>2</sub> O	64.8 %

Components (a<sub>1</sub>-a<sub>5</sub>) (= phase A) are homogenised separately and very carefully and are then, like components (b<sub>1</sub>)-(b<sub>3</sub>) (= phase B), heated separately to 75-80°C. Phase B is then added to phase A with vigorous stirring. With stirring, the mixture is allowed to cool.


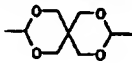

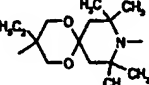
The sunscreen factor of this suntan cream is 6 (determined using the SPF analyser SPF 290 of Optometrix).

**Examples 5 to 33:**

Compositions of cosmetic formulations with the benzotriazole compounds given in Table 1.

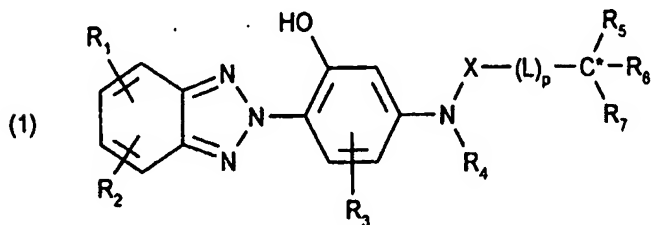
The remaining components and the preparation process correspond to Example 1.

Table 1:

Ex. No.	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	L	R <sub>5</sub>	R <sub>6</sub>	R <sub>7</sub>
5	H	5-F	H	H	CH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
6	H	5-Cl	H	H	CH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
7	H	5-F	H	H	CH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
8	H	H	H	CH <sub>2</sub> -COOCH <sub>3</sub>	CH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
9	H	H	H	CH <sub>2</sub> -COOCH <sub>3</sub>	CH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
10	H	H	H	CF <sub>2</sub> CF <sub>3</sub>	CH <sub>2</sub>	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
11	H	H	H	H	(CH <sub>2</sub> ) <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
12	H	H	6'-OH	H	CH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
13	H	H	6'-OH	C <sub>2</sub> H <sub>5</sub>	CH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
14	H	H	6'-OH	CH <sub>3</sub>	CH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
15	6-CH <sub>3</sub> O	5-CH <sub>3</sub> O	H	C <sub>2</sub> H <sub>5</sub>	CH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
16	H	5-CH <sub>3</sub> O	H	C <sub>2</sub> H <sub>5</sub>	CH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
17	H	5-Cl	H	sec-butyl	CH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
18	H	5-sec-C <sub>4</sub> H <sub>9</sub> O	H	sec-butyl	CH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
19	H	5-CH <sub>3</sub> O	H	sec-butyl	CH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
20	H	H	5'-Cl	sec-butyl	CH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
21	H	H	5'-Cl	sec-butyl	CH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
22	H	H	5'-F	sec-butyl	CH <sub>2</sub>	H	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>
23	6-F	5-F	H	CH <sub>2</sub> SO <sub>2</sub> O-s-C <sub>4</sub> H <sub>9</sub>	CH <sub>2</sub>	H	CH <sub>3</sub>	C <sub>4</sub> H <sub>9</sub>
24	H	5-s-C <sub>4</sub> H <sub>9</sub> S	H	sec-butyl	CH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
25	H	5-s-(C <sub>4</sub> H <sub>9</sub> )N	H	ethyl	CH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
26	H	H	H	H	CH <sub>2</sub> OCH <sub>2</sub> CH <sub>2</sub> O	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
27	H	H	H	H	(CH <sub>2</sub> OCH <sub>2</sub> CH <sub>2</sub> O) <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
28	H	H	H	H	CH <sub>2</sub> COOCH <sub>2</sub>	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
29	H	H	H	H		H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
30	H	H	H	H	CH <sub>2</sub> COOCH <sub>2</sub> CH(OCOCH <sub>3</sub> )CH <sub>2</sub> O	H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
31	H	H	H	H		H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
32	H	H	H	H		H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>
33	H	H	H	H		H	C <sub>2</sub> H <sub>5</sub>	C <sub>4</sub> H <sub>9</sub>

What is claimed is

1. Use of selected benzotriazole derivatives for protecting human and animal hair and skin from the harmful effects of UV radiation, which selected benzotriazole derivatives conform to formula



wherein

$R_1$ ,  $R_2$  and  $R_3$  are each independently of one another hydrogen; straight-chain or branched  $C_1$ - $C_{22}$ alkyl; hydroxy; carboxy; carbo- $C_1$ - $C_{22}$ alkoxy; nitro;  $C_2$ - $C_{22}$ alkylcarbonylamino;  $C_5$ - $C_8$ cycloalkyl; carbamoyl; sulfonyl; sulfamoyl; sulfonamido;  $C_2$ - $C_{22}$ alkylcarbonyloxy; cyano; halogen;  $C_6$ - $C_{12}$ aryl or  $C_4$ - $C_{12}$ heteroaryl which are unsubstituted or substituted by one or several  $C_1$ - $C_4$ alkyl;  $C_7$ - $C_{10}$ aralkyl which is unsubstituted or substituted by one or several  $C_1$ - $C_4$ alkyl;  $C_6$ - $C_{12}$ aryloxy; or a radical of formula



wherein

$A_1$  is straight-chain or branched  $C_1$ - $C_8$ alkyl;  $C_5$ - $C_8$ cycloalkyl;  $C_6$ - $C_{12}$ aryl which is unsubstituted or substituted by one or several  $C_1$ - $C_4$ alkyl; or  $C_7$ - $C_{10}$ aralkyl which is unsubstituted or substituted by one or several  $C_1$ - $C_4$ alkyl;

$m_1$  is 1 to 10;

Q is -O-; -S-; or -NH-; or

$R_1$  and  $R_2$ , together with the benzene ring of the benzotriazole, are a  $C_5$ - $C_{18}$ aryl ring or a  $C_4$ - $C_{18}$ heteroaryl ring, which rings are unsubstituted or substituted by  $C_1$ - $C_{22}$ alkyl or  $C_1$ - $C_{22}$ alkoxy;

$R_4$  is hydrogen;  $C_1$ - $C_{22}$ alkyl which is unsubstituted or substituted by 1 to 5 halogen atoms and/or which is interrupted by a -C(O)-O- or -SO<sub>2</sub>-O- group;

$R_5$ ,  $R_6$ ,  $R_7$  are each independently of one another hydrogen; halogen; cyano; straight-chain or branched  $C_1$ - $C_{22}$ alkyl; straight-chain or branched  $C_1$ - $C_{22}$ alkoxy;  $C_6$ - $C_{12}$ aryl; straight-

chain or branched C<sub>1</sub>-C<sub>22</sub>thioalkyl; mono- or di-C<sub>1</sub>-C<sub>22</sub>alkylamino; mono- or di-C<sub>6</sub>-C<sub>12</sub>-aryl amino; R<sub>5</sub> ≠ R<sub>6</sub> ≠ R<sub>7</sub>;

X is  $\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}-\text{O}- \end{array}$ , the carbonyl carbon atom being bound to the nitrogen atom of the  $\begin{array}{c} -\text{N}- \\ | \\ \text{R}_4 \end{array}$  moiety; or -SO<sub>2</sub>-;

L is a divalent radical consisting of 1 to 20 atoms; and

p is 0 or 1.

2. Use according to claim 1, wherein the compound of formula (1) is a 60:40 to 40:60 mixture of two enantiomers relative to the asymmetrical C\* atom.

3. Use according to either claim 1 or claim 2, which comprises using benzotriazole derivatives of formula (1), wherein

L consists of 1 to 20 atoms and is a straight-chain or branched alkylene group which may be interrupted by 1 to 5 oxygen, sulfur or nitrogen atoms or by a -C(O)-O- group which is unsubstituted or substituted by C<sub>1</sub>-C<sub>10</sub>alkoxy, C<sub>1</sub>-C<sub>10</sub>alkylcarbonyloxy, C<sub>1</sub>-C<sub>10</sub>alkyl sulfide, amino, mono-C<sub>1</sub>-C<sub>10</sub>alkylamino, di-C<sub>1</sub>-C<sub>10</sub>alkylimino or halogen; or the divalent radical of a 4- to 6-membered alicyclic ring or of a heterocyclic ring containing 1 to 3 hetero atoms.

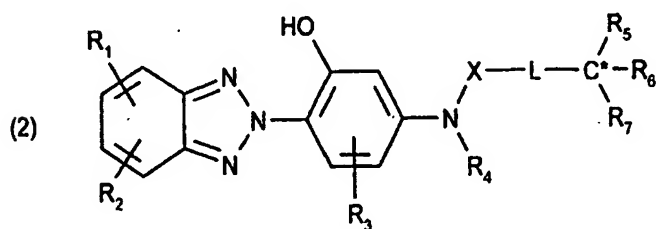
4. Use according to either claim 1 or claim 2, which comprises using benzotriazole derivatives of formula (1), wherein

L is a methine group which is unsubstituted or substituted by C<sub>1</sub>-C<sub>12</sub>alkyl or C<sub>1</sub>-C<sub>12</sub>alkoxy, amino, mono- or di-C<sub>1</sub>-C<sub>6</sub>alkylamino or halogen, wherein C<sub>1</sub>-C<sub>12</sub>alkyl or C<sub>1</sub>-C<sub>12</sub>alkoxy may be interrupted by 1 or 2 oxygen atoms.

5. Use according to any one of claims 1 to 4, wherein, in formula (1),

$R_5$ ,  $R_6$ ,  $R_7$  are each independently of one another hydrogen; or straight-chain or branched  $C_1$ - $C_{22}$ alkyl.

6. Use according to any one of claims 1 to 5, which comprises using benzotriazoles of formula



wherein

$R_1$  and  $R_2$  are each independently of one another hydrogen; halogen;  $C_1$ - $C_5$ alkyl;  $C_1$ - $C_5$ alkoxy; mono- or di- $C_1$ - $C_5$ alkylamino; or  $C_1$ - $C_5$ alkyl sulfide;

$R_3$  is hydrogen; hydroxy; or halogen;

$R_4$  is hydrogen;  $C_1$ - $C_5$ alkyl which is unsubstituted or substituted by 1 to 5 halogen atoms and/or which may be interrupted by a  $-C(O)-O-$  or  $-SO_2-O-$  group;

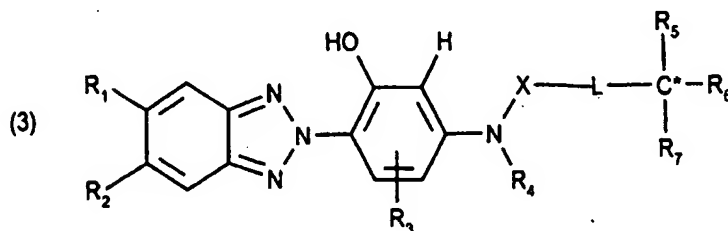
$L$  is a straight-chain or branched alkylene group which may be interrupted by 1 to 5 oxygen atoms or by a  $-C(O)-O-$  group which may be substituted by  $C_1$ - $C_{10}$ alkoxy or  $C_1$ - $C_{10}$ alkylcarbonyloxy; and

$R_5$ ,  $R_6$ ,  $R_7$  are each independently of one another hydrogen or  $C_1$ - $C_{10}$ alkyl;  $R_5 \neq R_6 \neq R_7$ ; and

$X$  is  $-\overset{\overset{O}{\parallel}}{C}-O-$ , the carbonyl carbon atom being bound to the nitrogen atom of the  $-\overset{\overset{R_4}{\mid}}{N}-$

moiety; or  $-SO_2-$ .

7. Use according to claim 6, which comprises using benzotriazoles of formula



wherein

$R_1$  and  $R_2$  are each independently of the other hydrogen; halogen;  $C_1$ - $C_5$ alkyl;  $C_1$ - $C_5$ alkoxy; or  $C_1$ - $C_5$ alkyl sulfide;

$R_3$  is hydrogen; halogen or hydroxy;

$R_4$  is hydrogen;  $C_1$ - $C_5$ alkyl which is unsubstituted or substituted by 1 to 5 halogen atoms and/or which may be interrupted by a  $-C(O)-O-$  or  $-SO_2-O-$  group;

$R_5$ ,  $R_6$ ,  $R_7$  are each independently of one another hydrogen or  $C_1$ - $C_{10}$ alkyl;  $R_5 \neq R_6 \neq R_7$ ;

$L$  is a straight-chain or branched alkylene group which may be interrupted by 1 to 5 oxygen atoms or by a  $-C(O)-O-$  group which may be substituted by  $C_1$ - $C_{10}$ alkoxy or  $C_1$ - $C_{10}$ alkylcarbonyloxy; and

$X$  is  $\begin{array}{c} O \\ || \\ -C-O- \end{array}$ , the carbonyl carbon atom being bound to the nitrogen atom of the  $\begin{array}{c} -N- \\ | \\ R_4 \end{array}$  moiety; or  $-SO_2-$ .

8. A cosmetic preparation, comprising at least one benzotriazole derivative of formula (1) as well as cosmetically compatible carriers or auxiliaries.

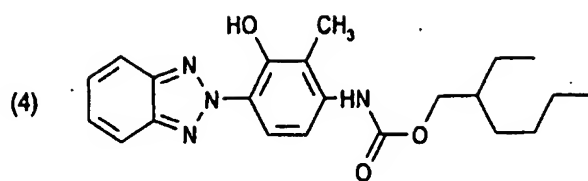
9. A cosmetic preparation according to claim 8, which comprises 0.25 to 15 % by weight, based on the total weight of the composition, of a benzotriazole derivative of formula (1).

10. Use of the preparation according to either claim 8 or claim 9 for protecting human and animal skin and hair from UV radiation.

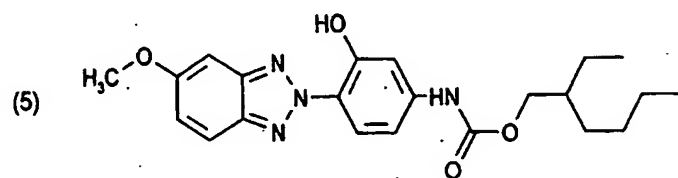
11. A process for treating human hair to protect it from the harmful effects of UV radiation, which comprises treating the hair with a shampoo, lotion, gel or emulsion for rinsing, before or after shampooing, before or after dyeing or removing the dye, before or after a perming or straightening process, with a lotion, foam or gel for setting, with a lotion, foam or gel for brushing or waving, with a hair lacquer, with a composition for perming or straightening hair, for dyeing or removing dye, which shampoo, lotion, gel, emulsion, foam, hair lacquer or composition for perming, straightening, dyeing or removing dye comprises a benzotriazole derivative of formula (1).

12. A compound of formula

- 21 -



13. A compound of formula



# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 97/06330

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 6 A61K7/42 C07D249/20

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JP 50 121 178 A (SUMITOMO CHEMICAL CO.) 22 September 1975 see the whole document & CHEMICAL ABSTRACTS, vol. 84, no. 6, 9 February 1976 Columbus, Ohio, US; abstract no. 035204, see abstract ---	1-13
X	GB 2 288 613 A (CIBA GEIGY AG) 25 October 1995 see the whole document ---	1
A	FR 2 194 442 A (RICHTER GEDEON VEGYESZET) 1 March 1974 see the whole document ---	1
-/--		

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

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Date of the actual completion of the international search

12 May 1998

Date of mailing of the international search report

18/05/1998

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# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 97/06330

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